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A SINGLE-STEP SYNTHESIS OF (±)-α-CUPARENONE[1]

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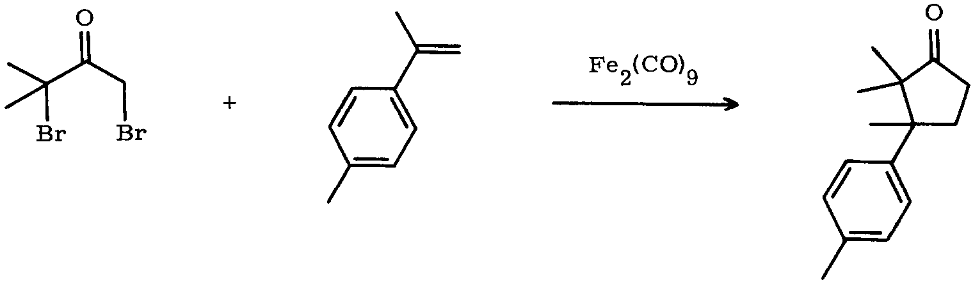
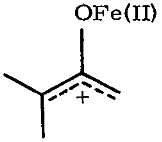
The iron carbonyl-promoted cyclocoupling reaction between α,α'-dibromo ketones and arylated olefins provides a new tool for the synthesis of 3-arylcyclopentanones.[2] We here describe a simple sesquiterpene synthesis based on this 3 + 2 → 5 reaction.

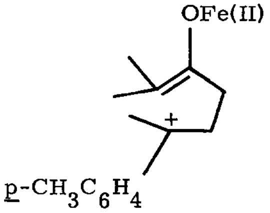
A mixture of 1,3-dibromo-3-methyl-2-butanone, 2-p-tolylpropene, and $Fe_2(CO)_9$ (1:4:1.4 mol ratio) in benzene was stirred at 55° for 17 hr under argon. After extractive workup and chromatographic separation there was obtained α-cuparenone (I) in 18% yield.[3] In addition, its regioisomer, 2,2,4-trimethyl-4-p-tolylcyclopentanone (II) (1.2%),[5] and some open-chain 1:1 adducts (1—2%) were formed. The remainder consisted mainly of intractable polymeric material. The yield of I is not very high but the method is quite expeditious.[6] This terpene has previously been prepared from 3-methyl-2-cyclohexenone and toluene through seven steps in only 3.3% overall yield.[8,9]



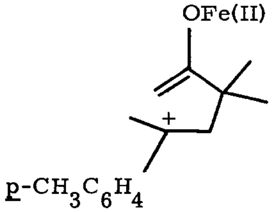
I



III



IV



V

The high regioselectivity of the cyclocoupling reaction, I/II = 94:6, is based on the relative stabilities of the reaction intermediates IV and V formed by electrophilic attack of the reactive oxyallyl species III[10] on the olefinic substrate. The intermediate IV, leading to I, that contains a dimethylated enolate moiety is much more stable than the regioisomer V containing a nonmethylated enolate.[11]

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3. The spectral properties of I were identical with the reported ones:[4] IR (CCl_4) 1740 cm^{-1} (C=O); NMR (CCl_4) δ 0.55 (s, 3 H, C(2)-CH_3 cis to aromatic ring), 1.11 and 1.23 (s, 3 H each, alicyclic CH_3), 1.7—2.9 (m, 4 H, CH_2), 2.32 (s, 3 H, tolyl CH_3), 7.12 (A_2B_2, 4 H, aromatic); mass spectrum m/e 216 (M^+).
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5. Spectral characteristics of II were: IR (CCl_4) 1740 cm^{-1} (C=O); NMR (CCl_4) δ 0.87, 1.13, and 1.35 (s, 3 H each, alicyclic CH_3), 2.08 and 2.28 (AB q, 2 H, J = 13 Hz, C(3)H_2), 2.30 (s, 3 H, tolyl CH_3), 2.37 and 2.87 (AB q, 2 H, J = 16.5 Hz, C(5)H_2), 7.07 (br s, 4 H, aromatic); mass spectrum m/e 216 (M^+).
6. The reaction using 1,1,3-tribromo-3-methyl-2-butanone in place of the dibromo ketone[7] gave after Zn/Cu couple reduction the undesired isomer II in 35% yield.
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